Molecular Testing of Bronchial Brushings

Policy Description

Percepta™ Bronchial Genomic Classifier is a test developed by Veracyte, a genomic diagnostics company (Veracyte, 2017). "Percepta Bronchial Genomic Classifier uses advanced genomic technology to help reduce the number of unnecessary surgeries and other procedures that can follow when potentially cancerous lung nodules or lesions are found on CT scans (Veracyte, 2017)."

Related Policies

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<th>Policy Number</th>
<th>Policy Title</th>
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Indications and/or Limitations of Coverage

Application of coverage criteria is dependent upon an individual's benefit coverage at the time of the request

1. A Gene expression profiling on bronchial brushings, including but not limited to Percepta Bronchial Genomic Classifier, is EXPERIMENTAL AND INVESTIGATIONAL for all indications, including in patients with indeterminate bronchoscopy results from undiagnosed pulmonary nodules.

Scientific Background

In the United States, over 1.5 million lung nodules are detected annually (Kearney et al., 2017). Low-dose computed tomography (LCDT) is the current standard for lung cancer screening. However, a limitation of the screening is that LCDT shows indeterminate pulmonary nodules which are not clearly defined as benign or cancerous. Assessment of a malignant nodule typically involves expensive biopsies whereas benign nodules may be only placed under close surveillance. Clinicians must often weigh the risk of a missed malignant diagnosis against performing an invasive procedure that may ultimately be unnecessary (Weinberger, 2019).
Introduced in 2015, Percepta Bronchial Genomic Classifier uses cells collected during bronchoscopy to detect genomic changes indicative of a cancerous nodule. Percepta “is designed to reduce the number of invasive biopsies and other procedures that can follow when suspicious lung nodules are found on computerized tomography (CT) scans (BU, 2015).” Percepta purports that it can add diagnostic value without an invasive biopsy (Veracyte, 2017).

The use of gene expression profiles to detect malignant and premalignant changes in samples of bronchial epithelial cells has generated sets of differential expression data associated with precancerous (Beane et al., 2017) and cancerous (Beane et al., 2011; Pavel et al., 2017; Spira et al., 2007) lesions.

Analytic Validity

Hu et al (2016) conducted studies to evaluate analytical performance of gene expression profiling test (Percepta test) using bronchial brushing specimens. The authors found that "analytical sensitivity studies demonstrated tolerance to variation in RNA input (157 ng to 243 ng). Analytical specificity studies utilizing cancer positive and cancer negative samples mixed with either blood (up to 10 % input mass) or genomic DNA (up to 10 % input mass) demonstrated no assay interference.” The authors concluded that “analytical sensitivity, analytical specificity and robustness of the Percepta test were successfully verified, supporting its suitability for clinical use (Hu et al., 2016).”

Clinical Validity and Utility

Whitney et al (2015) collected bronchial epithelial cells of 223 cancer-positive and 76 cancer-free subjects undergoing bronchoscopy for suspected lung cancer in a prospective, multi-center study. RNA from these samples was run on gene expression microarrays for training a gene-expression classifier. Out of the 232 genes whose expression levels in the bronchial airway were found to be associated with lung cancer, the authors built a classifier based on the combination of 17 cancer genes, gene expression predictors of smoking status, smoking history, and gender, plus patient age. The authors concluded that their gene classifier “is able to detect lung cancer in current and former smokers who have undergone bronchoscopy for suspicion of lung cancer. Due to the high NPV of the classifier, it could potentially inform clinical decisions regarding the need for further invasive testing in patients whose bronchoscopy is non-diagnostic (Whitney et al., 2015).”

Silvestri et al (2015) reported on the diagnostic performance of a gene-expression classifier. 639 current or former smokers undergoing bronchoscopy for suspected lung cancer enrolled in two multicenter prospective studies (AEGIS-1 and AEGIS-2) were evaluated. A gene-expression classifier was measured in epithelial cells to assess the probability of lung cancer. In AEGIS-1, the classifier had a sensitivity of 88% and a specificity of 47%. In AEGIS-2, the classifier had a sensitivity of 89% and a specificity of 47%. The combination of the classifier plus bronchoscopy had a sensitivity of 96% in AEGIS-1 and 98% in AEGIS-2. The authors concluded that “the gene-expression classifier improved the diagnostic performance of bronchoscopy for the detection of lung cancer. In intermediate-risk patients with a nondiagnostic bronchoscopic examination, a negative classifier score provides support for a more conservative diagnostic approach (Silvestri et al., 2015).”

Ferguson et al. (2016) conducted a randomized, prospective decision impact survey study to evaluate pulmonologist recommendations in patients undergoing workup for lung cancer who had an inconclusive bronchoscopy. The authors’ goal was to examine if a negative genomic classifier result that down-classifies a patient from intermediate risk to low risk (<10 %) for lung cancer would reduce the rate that physicians recommend more invasive testing among patients with an inconclusive bronchoscopy. The authors found that “invasive procedure recommendations were reduced from 57 % without the classifier result to 18 % with a negative (low risk) classifier result. Invasive procedure recommendations increased from 50 to 65 % with a positive (intermediate risk) classifier result.” The authors concluded that their results “support the potential clinical utility of the classifier to improve management of patients
undergoing bronchoscopy for suspect lung cancer by reducing additional invasive procedures in the setting of benign disease (Ferguson et al., 2016).”

Lee et al (2017) published Interim results from a large prospective registry of 665 patients undergoing diagnostic bronchoscopy. In a subset of 209 patients with an intermediate pretest risk of malignancy, Advanced bronchoscopic techniques were used in in 68% of cases. The BGC test results reclassified 74 patients as low risk. At 10 months post follow up the patients reclassified as low risk had a 40% relative reduction in the use of invasive procedures. They concluded that the BGC improves the sensitivity of diagnostic bronchoscopy for patients undergoing evaluation for lung cancer and can reduce the number if unnecessary invasive procedures.

Feller-Kopman et al (2017) assessed the cost effectiveness of bronchoscopy plus a genomic classifier versus bronchoscopy alone in the diagnostic work-up of patients at intermediate risk for lung cancer. They found that “Use of the genomic classifier reduced invasive procedures by 28% at 1 month and 18% at 2 years, respectively. Total costs and QALY gain were similar with classifier use ($27,221 versus $27,183 and 1.512 versus 1.509, respectively), resulting in an incremental cost-effectiveness ratio of $15,052 per QALY (Feller-Kopman et al., 2017).” They concluded that use of a genomic classifier was associated with meaningful cost reduction in invasive procedures.

Guidelines and Recommendations

American College of Chest Physicians

In 2013, the ACCP published evidence-based clinical practice guidelines for diagnosis and management of lung cancer (Detterbeck, Lewis, Diekemper, Addrizzo-Harris, & Alberts, 2013). The guidelines did not mention gene expression profiling as a potential diagnostic or screening tool.

National Comprehensive Cancer Network

The NCCN guidelines v4.2019 for Non-Small Cell Lung Cancer did not mention gene expression profiling as a potential diagnostic or screening tool (NCCN, 2019a).

The NCCN Guidelines v1.2019 for Small Cell Lung Cancer did not mention gene expression profiling as a potential diagnostic or screening tool (NCCN, 2019b).

European Society for Medical Oncology (ESMO, 2017)

ESMO does not make any mention of gene expression profiling in its guideline for assessment of lung nodules (Postmus et al., 2017).

State and Federal Regulations, as applicable

This test is considered a laboratory developed test (LDT); developed, validated and performed by individual laboratories. LDTs are regulated by the Centers for Medicare and Medicaid (CMS) as high-complexity tests under the Clinical Laboratory Improvement Amendments of 1988 (CLIA’88). As an LDT, the U. S. Food and Drug Administration has not approved or cleared this test; however, FDA clearance or approval is not currently required for clinical use.
Applicable CPT/HCPCS Procedure Codes

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<th>Code Description</th>
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Procedure codes appearing in Medical Policy documents are included only as a general reference tool for each policy. They may not be all-inclusive.

Evidence-based Scientific References


http://journal.chestnet.org/article/S0012369217321761/fulltext


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**Policy Implementation/Update Information**

1/1/20 New Policy

State and Federal mandates and health plan contract language, including specific provisions/exclusions, take precedence over Medical Policy and must be considered first in determining eligibility for coverage. The medical policies contained herein are for informational purposes. The medical policies do not constitute medical advice or medical care. Treating health care providers are independent contractors and are neither employees nor agents Blue KC and are solely responsible for diagnosis, treatment and medical advice. No part of this publication may be reproduced, stored in a retrieval system or transmitted, in any form or by any means, electronic, photocopying, or otherwise, without permission from Blue KC.